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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,309	06/06/2001	Masayoshi Mishina	55573	8081
21874	7590	05/26/2004	EXAMINER	
EDWARDS & ANGELL, LLP			PARAS JR, PETER	
P.O. BOX 55874			ART UNIT	
BOSTON, MA 02205			PAPER NUMBER	

1632

DATE MAILED: 05/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/786,309	Applicant(s) MISHINA ET AL.	
	Examiner Peter Paras, Jr.	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 March 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8, 10-13, 15-18 and 20-22 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8, 10-13, 15-18, and 20-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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Applicant's amendment received on 3/3/04 has been entered. Claims 9, 14, and 19 have been cancelled. Claims 8, 10-13, 15-18 and 20-22 have been amended. Claims 8, 10-13, 15-18 and 20-22 are pending and are under current consideration.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The previous rejection of claims 8-18 under 35 U.S.C. 112, first paragraph, is withdrawn in of the claim amendments.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The previous rejections of claims 8-22 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn in light of the claim amendments.

The following new grounds of rejection under 35 U.S.C. 112, second paragraph are necessitated by the claim amendments:

Claims 8, 10-13, 15-17, 18 and 20-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8, 13 and 18 are indefinite as written. The claims embrace the step of subjecting an irradiated sperm to artificial fertilization. The claims are indefinite because neither the specification nor the art teaches fertilization of sperm in any context. Sperm are normally known to fertilize oocytes. Appropriate correction is required. Claims 10-12, 15-17 and 20-22 depend from claims 8, 13 and 18 respectively.

Claim 8 is incomplete as written. The claim is directed to a method of mutating a gene of a vertebrate animal. However, the method steps do not relate back to the preamble in a positive process. For example, the method steps do not even recite mutation of a gene. Appropriate correction is required. Claims 10-12 depend from claim 8.

Claim 13 is incomplete as written. The claim is directed to a method of preparation of a mutated gene of a vertebrate animal. However, the method steps do not relate back to the preamble in a positive process. For example, the method steps do not even recite mutation of a gene. Claims 15-17 depend from claim 13.

Claim 18 recites the limitation "the treated germ cell" in step b. There is insufficient antecedent basis for this limitation in the claim. Claims 20-22 depend from claim 18.

Claim 18 recites the limitation "the mutated gene" in steps d, e and f. There is insufficient antecedent basis for this limitation in the claim. Claims 20-22 depend from claim 18.

Claim 18 recites the limitation "the said differences of phenotype" in step f. There is insufficient antecedent basis for this limitation in the claim. Claims 20-22 depend from claim 18

Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps of creating a mutant animal after artificial fertilization. Claims 20-22 depend from claim 18.

Claim 18 is indefinite as written. The claim is directed to a method for analyzing a function of a gene of a vertebrate animal. The claim requires 1) comparing phenotype of a mutant having the mutated gene with that of a wild-type to find the difference of phenotype between the mutant and the wild-type and 2) analyzing the functions of a gene of the vertebrate animal corresponding to the mutated gene from the said differences of phenotype. The claim is indefinite because the comparison step requires only a mutant and wild-type of an unknown entity. It is not understood what mutant and wild-type are referring to as recitation of such is broader than "vertebrate animal". Moreover, the claim is confusing as the analysis step relies on differences in phenotype

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between the mutant and wild-type to determine the function of a gene of a vertebrate animal. It is not understood how phenotypic differences between mutant and wild-type of unknown entity relate to the function of vertebrate gene. Appropriate correction is required. Claims 20-22 depend from claim 18.

Claim 18 is indefinite as written. The claim embraces a step directed to determining the mutated gene. The claim is indefinite because the specification has not defined the claim limitation "determining the mutated gene". It is unclear how a gene can be determined. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 8, 10-13, 15-18 and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chakrabarti et al (Genetics, 1983, 103: 109-123), Grunwald et al #1 (Genet. Res., 1991, 59: 93-101) and Grunwald et al #2 (Genet. Res., 1991, 59: 103-116) taken with Thomas et al (Mol. Cell. Biol., 1996, 16(5): 2537-2544). The previous rejection is maintained for the reasons of record advanced on pages 7-9 of the Office action mailed on 10/27/03.

Applicant's arguments filed 3/3/04 have been fully considered but they are not persuasive. Applicants assert that none of Chakrabarti, Grunwald #1, or Grunwald #2 teach or suggest mutating a gene by incorporating a small deletion in a vertebrate's genome or cloning such a mutated gene by the methods provided by the invention. See pages 6-7 of the amendment.

In response, the Examiner asserts the claims as amended do not require mutating a gene by incorporating a small deletion in a vertebrate's genome or cloning such a mutated gene. Therefore, the relevance of these arguments is not understood. In any event, Thomas teaches use of psoralens in conjunction with near UV light to induce genetic mutations. As set forth on page 9 of the Office action mailed on 10/27/03, Thomas teaches that among the mutations induced by psoralen/UV light are deletions of single A:T base pairs, which are clearly small deletions. Furthermore, the steps of the methods do not recite induction of a mutation in a gene by psoralen/UV light. The recitations "mutating a gene" (claim 8) and "mutated gene" (claim 13) have not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

In addition, Chakrabarti et al correlated the effects of mutating the gol-1 gene with a mutant phenotype; the mutant gol-1 zebrafish comprise both pigmented and unpigmented patches in the retina of the eye. See pages 114-115. Such can be interpreted to read on analyzing the function of a gene (claim 18). Finally, the claim limitation (claim 18) "determining the mutated gene" is not interpreted to mean cloning the mutated gene. It is clear that determining and cloning do not have the same meaning. The meaning of "determining" is not clear in the context of the claim as written. See the rejection under 112, 2nd paragraph above.

Applicants assert that Thomas neither suggests nor teaches small deletions in a vertebrate genome induced by a psoralen derivative and UV light. See page 7 of the amendment.

In response, the Examiner reiterates that Thomas has taught deletions of single A:T base pairs, which are clearly small deletions. See page 9 of the Office action mailed on 10/27/03.

Applicants assert that there is no motivation to combine the references to arrive at the claimed invention. See pages 7-8.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re*

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Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, mutagens such as psoralens, particularly 4, 5', 8-trimethylpsoralen, were routine in the art as evidenced by Thomas. In addition, psoralens represent a difference class of mutagens capable of inducing different types of mutations, from other known mutagens as pointed out by Thomas, such as T:A—C:G transitions, transversions at C:G base pairs, and deletions of single A:T base pairs. The collective teachings of Chakrabarti, Grunwald #1, and Grunwald #2 suggest that it was an art-recognized goal to mutate genes of zebrafish, for analyzing gene function, through the use of different mutagens. Given the teachings of all the cited references as a whole, the ordinarily skilled artisan would have been sufficiently motivated to use psoralens, such as 4, 5', 8-trimethylpsoralen, to mutate genes in zebrafish in accordance with the methods of Chakrabarti, Grunwald #1, and Grunwald #2.

Accordingly, the previous rejection is maintained for the reasons of record.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is (571) 272-0732. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 571-272-0804. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Official Fax Center number is (703) 872-9306.

Inquiries of a general nature or relating to the status of the application should be directed to Dianiece Jacobs whose telephone number is (571) 272-0532.

Peter Paras, Jr.

**PETER PARAS, JR.
PRIMARY EXAMINER**

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